REMARKS

The foregoing amendment amends claims 1, 9, 14, 15, 20 and 26-28. Pending in the application are claims 1-47, of which claims 1, 15, 42 and 43 are independent. Claims 42-47 have been withdrawn pursuant to a Restriction Requirement. The following comments address all stated grounds for rejection and place the presently pending claims, as identified above, in condition for allowance.

Claims 1 and 15 are amended to specify that the virtual wall has a dead volume that is less than one nanoliter. Support for the amendment can be found throughout the original application as filed, at least, for example, on page 21, lines 15-18.

Claims 1, 9, 14, 15 and 26-28 are amended for purposes of clarity only, for reasons not related to patentability. Namely, claims 1, 9 and 15 are amended to change the word "channel" to the word ---microchannel--- to be consistent with the language of the claims.

Claim 14 is amended to change the word "methods" to ---method---.

Claims 26-28 are amended to depend from claim 25, rather than claim 15. *No new matter is added.*

Amendment and/or cancellation of the claims is not to be construed as an acquiescence to any of the objections/rejections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicant reserves the right to pursue the claims as originally filed, or similar claims, in this or one or more subsequent patent applications.

<u>Response to Restriction Requirement</u>

Applicants confirm the election of Group I in response to the Restriction Requirement.

<u>35 U.S.C. 112 Rejection</u>

Regarding the rejection of claim 23 for being indefinite, Applicants respectfully submit that the claim is clear and definite to one of ordinary skill in the art in light of the specification. The encapsulant may comprise any suitable material that will cover the virtual wall without

mixing with the liquid forming the virtual wall, i.e., the encapsulant is immiscible with the liquid in the microchannel. The type of material used for the encapsulant depends on the type of liquid in the microchannel. For example, if the liquid in the microchannel is an aqueous solution, the encapsulant will comprise a hydrophobic material that will not mix with the aqueous solution. Because suitable materials for forming the encapsulant would be known in the art, Applicants submit that the claim is clear and definite, and request that the rejection be reconsidered and withdrawn.

35 U.S.C. 102 Rejections

In the Office Action, the Examiner rejects claims 1-22 and 24-41 under 35 U.S.C. 102(e) as being anticipated by Dubrow (U.S. Patent Number 6,251,343). Applicants respectfully traverse the rejection and submit that the claims distinguish patentably over the Dubrow reference. The Dubrow reference does not teach or suggest a fluid interface port that is sized and dimensioned to form a *virtual wall*. In fact, the Dubrow reference teaches *away* from forming a fluid interface port in a microchannel side wall that forms a virtual wall when the channel is filled with liquid.

The Dubrow reference is directed to a microfluidic device comprising a body structure including a channel network and a cover layer coupled to the body structure. An upper layer of the body structure includes ports in the form of reservoirs for communicating with the channels. The cover layer includes apertures that are positioned so as to align with the reservoirs of the body structure when the microfluidic device is assembled. The ports 106 of Dubrow are not sized and dimensioned to form a virtual wall when the channel network is filled with a liquid, as recited in independent claims 1 and 15.

As set forth in the specification, in particular on page 17, lines 10-30 and page 21, lines 7-18, a "virtual wall" refers to a meniscus formed by a liquid in a fluid interface port formed in the side wall of the microchannel, which essentially replaces the removed portion of the side wall that defines the fluid interface port. A virtual wall provides fluid access to the interior of a microchannel without influencing the overall liquid flow through the microchannel, i.e. the flow of liquid in the microfluidic system having a virtual wall is substantially identical to the flow of liquid through an identical microfluidic system in which no virtual wall is present. A virtual

wall forms a *direct* interface between the microchannel interior and the microchannel exteri r, allowing direct access to the liquid in microchannel without introducing dead or unswept volume in the microchannel. The virtual wall also serves to seal liquid inside of the microchannel through a range of pressures in the microchannel.

The virtual wall is formed within an aperture defining a fluid interface port having cross sectional dimensions such that resulting capillary forces retain liquid within the microchannel. As described on page 10, lines 30-33, a fluid interface port forming a virtual wall generally has a diameter of between about 0.1 μm and about 200 μm and preferably between about 25 μm and about 125 μm and most preferably between about 50 μm and about 100 μm.

As set forth in independent claims 1 and 15, a virtual wall also has a relatively low dead volume, i.e., less than about one nanoliter. "Dead volume" refers to the volume of liquid retained in the fluid interface port (i.e. the volume of liquid the fluid interface port holds that is not flushed through the fluid interface port by the flow field of liquid through the microchannel). The relatively small dead volume provided by the virtual wall results in a <u>direct</u> fluid interface allowing <u>direct</u> injection of a precise volume of sample into the interior of the microchannel from the exterior of the microchannel. The ability to directly inject sample into the microchannel due to the low dead volume of the fluid interface port provides improved control over the amount of sample that is injected into the microchannel, allows efficient use of sample, and significantly reduces waste of the sample. Furthermore, the direct injection provided by the very small dead volume reduces or prevents cross-contamination between different samples and allows a second substance to be directly injected into the system immediately after a first substance without requiring flushing of the fluid interface port.

In contrast to the claimed invention, the Dubrow reference employs a sample <u>reservoir</u> for introducing a fluid sample to a microchannel. The sample reservoir forms an *intermediate* structure for introducing a sample, rather than a *direct* fluid interface port. The sample reservoir is incapable of forming a virtual wall, because the diameter of the sample reservoir is significantly, i.e., several times, *larger* than the diameter of an associated channel, as shown in Figure 1. While the Dubrow reference is silent as to the *exact* cross-sectional dimension of the

ports 106, it can be inferred from the Figures and from the specified relationship between the depth and volume of the ports (see column 8, lines 20-33), that the diameter of the ports 106 is much larger than the diameter range that is specified in the present application as being suitable for forming a virtual wall, i.e., between about 0.1 μm and about 200 μm. The port forming the sample reservoir does not form a virtual wall, because the opening is too large to produce capillary forces that are capable of retaining liquid within the microchannel. Rather, liquid extends from within the microchannel and fills the reservoir.

In fact, the Dubrow reference teaches *away* from a fluid interface port of a microchannel that forms a virtual wall having a dead volume of less than about one nanoliter. The Dubrow reference, as set forth in column 8, lines 4-33 seeks to increase the fluid volume capacity of a reservoir, which expressly teaches away from the claimed invention. The Dubrow reference states that the volume capacity of the reservoir is preferably at least five microliters, which is significantly larger than one nanoliter.

The dead volume of the sample reservoirs in Dubrow is significantly large relative to the size of the channels. In order to introduce a fluid sample into a channel interior, the fluid sample must first pass through the dead volume in the sample reservoir 106. The large dead volume of at least 5 microliters leads to dispersion of the sample, a time delay between the time of injection and the time when the sample enters the microchannel, injection inefficiency, potential cross-contamination between different samples and difficulty controlling the amount of sample that actually reaches the microchannel. These problems are avoided or reduced by the use of the fluid interface port forming a *virtual wall*, as recited in independent claims 1 and 15.

The dependent claims recite additional patentable features that are neither taught nor suggested in the cited Dubrow reference. For example, claims 8-10 and 20 recite a hydrophobic patch disposed *in* the microchannel. The Dubrow reference describes using a hydrophobic material on an outside surface of the upper layer to prevent fluid from escaping the reservoirs. However, the Dubrow reference does not teach or suggest using a hydrophobic material on an *interior* surface of a microchannel, as recited in claims 8-10 and 20.

The Dubrow reference also does not teach or suggest a covering layer for *covering* and *sealing* a fluid interface port formed by an aperture in a side wall of a microchannel, as recited in claim 24. The upper layer of Dubrow includes apertures specifically designed to provide *access* to the sample reservoirs, which teaches away from covering and sealing a fluid interface port.

The Dubrow reference also fails to teach or suggest a covering layer disposed *in* a fluid interface port, as recited in claims 25-28. Rather, the upper layer in Dubrow is *adjacent to* but outside of the sample reservoirs.

The Dubrow reference also fails to teach or suggest a heater disposed in a microchannel, as recited in claim 38.

The Dubrow reference also does not teach or suggest using a fluid interface port to *eject* a sample from a microchannel interior. Specifically, the Dubrow reference does not teach or suggest a pressure pulse generator for applying a pressure pulse to a fluid when disposed in the microchannel to eject a droplet of the fluid from the fluid interface port, as recited in claims 40-41.

For at least these reasons, pending claims 1-41 distinguish patentably over the Dubrow reference and all claims are clear and definite. As such, Applicants respectfully request that the rejections of the claims under 35 U.S.C. 112 and 35 U.S.C. 102 be reconsidered and withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. If, however, the Examiner considers that obstacles to allowance of these claims persist, we invite a telephone call to Applicant's representative.

Applicants believe no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. TGZ-001C from which the undersigned is authorized to draw.

Dated: April 21, 2004

Respectfully submitted,

By [signature]

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